NATIONAL JOURNAL OF MEDICAL RESEARCH

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NATIONAL JOURNAL OF MEDICAL RESEARCH
Volume 7 │ Issue 2 │ Pages 79 – 105 │ April - June 2017

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Original Article

ORIGINAL ARTICLE

COMPARISON OF EARLY MANAGEMENT OF COMPOUND GRADE 2 AND 3A (GUSTILO-ANDERSON) FRACTURES OF TIBIA SHAFT USING PRIMARY INTRAMEDULLARY NAILING AND PLACEMENT OF ANTIBIOTIC BONE-CEMENT BEADS, WITH THAT OF EXTERNAL FIXATOR APPLICATION

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ABSTRACT

Introduction: Compound fractures of tibia have been conventionally managed by debridement and external fixation, followed by intra medullary nailing or Ilizarov technique after few months. Definitive surgery is delayed in the early stages, as it may cause infections and additional soft tissue damage. But external fixators have their own set of complications. Hence a technique of antibiotic coated intramedullary nail (locked or unlocked) has been advocated.

Methodology: Total 30 patients with grade 2 & 3 A (Gustilo-Anderson) compound tibia fractures were selected for the study. Group 1 was operated with antibiotic coated intramedullary nails. Group 2 was operated with external fixators application and later with intra medullary nailing.

Results: The infection rate after nailing was 6.67% in group 1 (1out of 15) and 40% (6 out of 15) in group 2 (p=0.02 i.e. statistically significant).The timing to healing (cortical bridging) was 4.5 months (2 - 8.5months) in group 1 and 7.5 (3-18) months in group 2. (p=0.02i.e. statistically significant).The overall complication rate was 60% (9/15 cases) for group 2 and 26.67% (4/15 cases) for group 1 (p=0.03 i.e. statistically significant).Results of primary nailing with antibiotic impregnated cement are superior to delayed nailing after initial external fixation.

Conclusion: Primary nailing with antibiotic impregnated cement method is biologically active with greater advantages compared with existing methods of treatment in grade 2 & 3A compound tibia fractures. Clinical results are better with a lower infection rate and a less hospital stay.

Keywords: Compound Fractures, Tibial shaft, Intramedullary Nailing, Antibiotic Bone-cement Beads

INTRODUCTION

Compound tibia fractures comprise 25% of tibia fractures and are on rise due to high energy trauma due to road traffic accident, industrialization etc. These fractures are managed conventionally by emergency debridement and application of external fixation devices, followed by a definitive treatmentafter soft tissue healing, that may take a few weeks to months.[1,2] A technique of antibiotic coated intramedullary nailing (locked or unlocked) has also been advocated and practiced at some centers, though it requires under-sizing of the nail by 2 mm or so.[3]

Microbial contamination during compound injuries is mostly by gram negative rods and gram positive staphylococci and sometimes the MRSA. Topical therapy by incorporating heat resistant antibiotic in polymethacrylate cement, which is then placed in wound, is becoming popular. There is extensive literature about debridement within 24 hours for compound tibia fractures and is very effective to reduce the rate of infection.[1,4,5,6]

There is also extensive literature available that primary nailing in compound tibia fracture within 24 hours is effective in many patients for early fracture healing.[7,8,9,10] Negative pressure system such as Vaccum Assisted Closure (VAC) prevents desiccation of cortical bone and has also been recommended.[11] Risk of reoperation is 18% in unreamed nailing alone, along with risk of non union and deep infection.[9] Theoretically, reaming of the medullary canal and placement

of large nail will give better biomechanical stability. However concern is about deterioration of endosteal blood supply from reaming. There are many studies which compared reamed and unreamed nails and formed no statistical difference with regards to time to union, rate of union, infection and frequency of implant breakage (nail).[9,12] Most surgeons feel immediate intramedullary nailing poses an increased risk of septic complication and delayed nailing after external fixation could decrease this risk. There are many studies which show plating has higher failure rate and complications in compound tibia fractures and hence should not be done.[10,13,14]

Ilizarov ring fixation though proven useful, has many disadvantages like steep learning curve and are heavy implants, and so are reserved for non-unions or malunions, rather than primary fixation. Hence nailing remains only viable option with or without antibiotic cement, primary or delayed (after external fixator application). Antibiotic cement decreases local infection but the application of cement decreases the diameter of nail. Hence we preferred antibiotic beads over antibiotic impregnated nail. We wanted single surgery as far as possible, and hence did not do external fixation prior to nailing. That is why we decided to do primary unreamed intramedullary nailing with antibiotic beads for compound tibia 2,3A fractures.

METHODOLOGY

The present study was a prospective cohort studies from 2012 to 2014. Total 30 patients with Grade 2&Grade 3A Gustilo Anderson compound fractures of Tibial shaft which came to different hospitals in Pune district attended by 2 surgeons were selected for study. Patients with segmental fractures, fractures with significant bone loss, grade 3B & C tibia fracture, degloving injuries and patients with life threatening injuries were excluded from the study.

Permission was obtained from ethical committee of the institutional to conduct the study. Informed written consent of all the participants were obtained before enrollment. Those who were not willing to give written consent were not included in the study.

Group 1: Patients were operated under suitable anesthesia after being made hemodynamically stable. After debridement, intramedullary nail (V-nail or interlocking nail) of appropriate size was selected. Unreamed nailing procedure was performed as recommended using medial para-patellar approach. Antibi-

otic mixed polymethacrylate cement beads were prepared over thin stainless steel wire during the surgery and inserted through the wound. Due to wound size limitations most often only single beads chain of 3-5 beads could be inserted. One end of bead chain was kept out of wound for easy identification and removal after 6-8weeks. Antibiotics commonly used were Vancomycin 2gm or Gentamicin 320mg. After insertion of bead chain, wound closure was done. Postoperatively, patients were given limb elevation, IV antibiotics, and intravenous fluids for about 5 days. Suture removal was done after 12-14 days. Some patients in whom locking was not done were given above knee slab for about 6 weeks. Patients were mobilized on crutches but not allowed to bear weight till radiological signs of union were seen on X-ray. Patients were followed up for 1 year with 2 monthly X-rays.

Group 2: After debridement of the compound fractures, external fixator was applied and repeated dressings and IV antibiotics were given for about 12-14 days. After the wounds were healthy or healed, delayed intramedullary nailing was done. No beads were used as wound almost healed them.

Both groups of patients were given prophylactic antibiotics for 5 days and we're discharged between 6 to 12th days after nailing. Weight bearing was permitted with crutches after X-rays showed signs of healing.

RESULTS

There were total 30 patients enrolled in the study and out of which 15 were included in Group 1 and 15 were included in Group 2. Mean age of patients of group 1 was 47 years (18-74 yrs). And of group 2 was 40 years (22-77yrs). In group 1 there were 13 male and 2 female patients and in group 2 there were 10 male and 5 female. This difference was not statistically significant (p=0.10)

The mean follow up was 2.1 yrs (4 months to 2 yrs) for group 1, and 2.4 yrs (5 months to 4 yrs) for group 2 (p=0.19). The infection rate after nailing was 6.67% in group 1 (1out of 15) and 40% (6 out of 15) in group 2. This difference was statistically significant (p=0.02). The average time to heal (cortical bridging) was 4.5 months (2-8.5 months) in group 1 and 7.5 (3-18) months in group 2. (p=0.02 i.e. statistically significant). The overall complication rate was 60% for group 2 and 26.67% for group 1. This difference was statistically significant (p=0.03).

Table 1: Post operational condition of patients

Variable	Group 1	Group 2	p-Value
Infection Rate	1 (6.67%)	6 (40%)	0.02
Average time to heal	4.5 months	7.5 months	0.02
Overall complication rate	4 (26.67%)	9 (60%)	0.03

Table 2: Different types of Complications in both the groups

Complications	Group 1 (n=15) (%)	Group 2 (n=15) (%)
Non union	1 (6.67)	0
Nail Infection	1 (6.67)	6 (40.0)
Nail Breakage	1 (6.67)	1 (6.67)
Fat embolism	1 (6.67)	0
Knee stiffness	0	2 (13.33)
Total	**4 (26.67)**	**9 (60.0)**

Table 2 shows difference complications in both groups. In group 1, total 4 (26.67%) patients got complications. There was one case of each of non union, nail infection, nail breakage and patient developed fat embolism. Nonunion patient had to undergo Phemister grafting and cast. One nail breakage patient had to undergo nailing again with wider interlocked nail. Fat embolism patient was managed by medical treatment. Nail infection in one patient decreased after nail removal after healing of fracture (till then patient was on antibiotics).

In group 2, there were total 9 (60%) got complications. Two patients had knee stiffness, six had nail infections and one had nail breakage. One nail breakage was managed by revision nailing. 4 cases of nail infection required antibiotics cement beads and or antibiotic impregnated cement nails. 2 cases could be managed by antibiotics for 8-10 months followed by nail removal after fracture healing. However one patient had chronic fistulae formation and refused further surgery.

A new method of treatment is used which biologically active with greater advantages compared with existing methods of treatment. Clinical results are excellent with a lower infection rate with less hospital stay and treatment costs. Antibiotic impregnated cement beads as compared to group in which delayed nailing was done after initial external fixation (p=0.02) significantly. Time to healing was less in primary nailing with beads group than delayed nailing group.(p0.02)Overall complication rate was significantly less in primary nailing with beads group as compared to delayed nailing group (p=0.03).Lower hospital stays obvious as there is no delay in nailing in primary compared to delayed nailing group. This brings down treatment cost.

DISCUSSION

It has been estimated that more than 4.5 million open tibia fractures occur per year in India.[2] These fractures have significant morbidity, as the potential for contamination is high. Gustilo classification has been most widely used. Infection risk has been reported to be 0-2% for type 1 and 2-10% for type-2fractures & 10-50% for type 3 fractures.[14,15] With systemic antibiotics given within 3hrs of injury, risk of infection decreases 6-fold. With the propensity for gram positive infections, IV Cephalosporins are preferred. However for Type 3 fractures, additional coverage for gram negative organisms and anaerobic organisms is advised. General consensus is to maintain antibiotic coverage until wound is closed. Open fractures should be taken up for surgery on emergency basis using appropriate surgical judgment.[7] Surgical intervention with irrigation and meticulous debridement of injury decreases contamination and infection.[16] Recent studies have shown that open fractures are often contaminated with nosocomial organisms (I.e. pseudomonos) and that early closure may help prevent these infection.[7,15] Early stabilization of open fractures provide length, alignment, and rotation restoration which prevents further damage from mobile fracture fragments. This decreases soft tissue dead space and infection. The surgeon has many choices for fixation including external fixation, intramedullary nails and plates. There are many studies which shows plating has higher failure rate and complication in compound tibia fracture.[13]Hence we preferred to carry out study with external fixator and intramedullary nail only. However there are many studies which show external fixation alone has high failure rate as regards union and hence is often used only as temporary fixation device for wound management.[13,10,17,18] Hence delayed nailing after initial external fixation is often employed and literature studies shows that infection in compound fracture tibia nailing can be brought down after initial external fixation. Ilizarov fixation can be used as definitive fixation but is cumbersome, heavy, has a steep learning curve and is commonly used for malunion or nonunion cases.[19]Considering these literature studies we carried out comparative studies between delayed nailing after external fixation and primary nailing. To decrease infection we decided to use local antibiotic delivery system of heat stable antibiotic polymethacrylate beads with primary nailing. We prepared the beads intra operatively over 24 number of stainless steel wires, and inserted it through fractures wound. We prepared Vancomycin plus Gentamicin beads and retained it in autoclaved container in aseptic environment for use in few other cases. Hence we could use prepared beads from 40gm cement,2gm Vancomycin, 320 mg Gentamicin in almost 5 compound fractures on an average. Hence this treatment becomes economical also. As reamed nailing has increased infection chances in compound fractures we preferred unreamed nailing. Antibiotic cement coated nails are usually made with 8-10 mm diameter and don't have adequate resistance to fatigue and bending forces. Also cement around such nails is prone to decoupling and jamming during insertion and extraction. Hence we did not use them and went ahead with beads as they were economical also. Newer an-

tibiotic delivery system like bioabsorbable calcium sulfate / phosphate is costly and we did not use them.

CONCLUSION

Results of primary nailing with antibiotic impregnated cement beads are superior to delayed nailing after initial external fixation. Hence this method of treatment is biologically active with greater advantages compared with existing methods of treatment in grade 2,3A compound tibia fractures clinical results are excellent with a lower infection rate may less hospital stay.

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ORIGINAL ARTICLE

PULMONARY FUNCTIONS IN ADOLESCENTS WITH SICKLE CELL ANAEMIA: A CASE-CONTROL STUDY

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ABSTRACT

Introduction: Sickle cell diseases are one the commonest hemoglobinopathies in the central and southern India. About 20-30% deaths in Sickle cell anaemia (SCA) patients occur due to respiratory disorder. Studies had shown that highest mortalities in Sickle cell disease (SCD) patients is due to pulmonary complications. Pulmonary function test (PFT) assess the functional status of respiratory system so the study was planned to determine the changes in lung functions in SCA adolescent patients and to compare it with age, gender and body mass index (BMI) matched healthy adolescent individuals using Spirometry.

Material and methods: 60 adolescent subjects (30 cases (SCA) and 30 controls) were included in the study whose pulmonary function test parameters using spirometry were measured.

Results: 22 (73.4%) had abnormal spirometric results, 18 (60%) had restrictive pattern, 2(6.6%) had obstructive pattern, 2(6.6%) had mixed pattern and 8 (26.6%) had no abnormality.

Conclusion: Pulmonary functions are significantly decreased in sickle cell anaemia adolescents. Possible restrictive pattern is the predominant spirometric abnormality in these patients.

Keywords: Sickle cell anemia, Sickle cell disease, Spirometry, Pulmonary function test, restrictive abnormality

INTRODUCTION

Sickle-cell disease (SCD) is one of the commonest hemoglobinopathies in the central and southern India.[1] It is a genetically transmitted hemoglobinopathy which is autosomal recessive in nature which may affect any organ or system of the body.[2] Hemolytic anaemia, granulocytosis, vaso-occlusion, acute chest syndrome (ACS), pulmonary infarction and pneumonia are seen in SCD patients[3]. Pulmonary function test (PFT) assesses the functional status of respiratory system.[4] Spirometry detects, quantifies & monitors the disease that limits ventilatory capacity of the lung.[5] Adolescent group, which consists of children in the age group of 10-19 years constitutes about 23% population of India.[6] About 20-30% deaths in Sickle cell anaemia (SCA) patients occur due to respiratory ailments that requires hospitilization.[7] Many complications in SCA are manifested in childhood and adolescence group which may result in repeated lung damages caused by episodes of pulmonary vasocculsion including pulmonary hypertension, pulmonary vasocculsion and ACS.[7] Studies have shown that highest mortalities in SCD patients is due to pulmonary complications such as pulmo-

nary hypertension and ACS.[8] Considering the number of circulatory and pulmonary dysfunctions in SCA patients, the lung functions are important to analyse in these patients since they remain underdiagnosed by physicians. With this background, the current study was planned to determine the changes in lung functions in SCA adolescent patients using spirometry.

METHODOLOGY

The study was conducted during July 2012 to December 2014. The study was carried out after approval from the institutional ethical committee and with fully informed written consent from the subjects, in a tertiary care teaching hospital in central India. This was an observational case control study. The following two groups of subjects were included: 30 adolescent SCA patients and 30 healthy control subjects. A total of 60 consecutive subjects were included in the study depending on the criteria till the desired sample size of each group was met. The patients were recruited as per the following criteria:1. SCA: Adolescent boys and girls aged between 10 to

19 years of age diagnosed with HbSS pattern SCA. 2. Healthy control subject: Age, gender and body mass index (BMI) matched healthy adolescent who was a 1st or 2nd degree cousin of sickle cell patients and having confirmed negative sickling test. Subjects with cardiac disorder, history of smoking, gross abnormalities of the vertebral column or thoracic cage, neuromuscular disease, malignancy, known infection with human immunodeficiency virus (HIV), acute respiratory infections, extreme BMI, history of any previous pulmonary and cardiac surgery or clinical examination suggestive of any other respiratory or cardiac comorbidity were excluded from the study. Also, acute chest syndrome was a specific exclusion criterion for the SCA group. After detailed clinical assessment all the subjects underwent spirometry (Spirometer - Medical Graphics Corporation, USA; Software: Breeze Suite Version 6.2C). The spirometry was performed and interpreted as per the ATS criteria. The spirometric parameters that were recorded were forced expiratory volume in 1st second (FEV1), forced vital capacity (FVC), FEV1 /FVC, Peak expiratory flow rate (PEFR) and Forced expiratory flow - 25% to 75% (FEF25-75%) along with Maximum voluntary ventilation MVV.

Statistical analysis: The pulmonary function test values of all the subjects were analysed. Percentage predicted values of the PFT parameters were recorded except for FEV1/FVC where absolute values were recorded. Following variables were used for statistical analysis: FVC, FEV1, FEF25-75, PEF and MVV. The data was analysed statistically by using graph pad instat 3 software. Various statistical measures such as mean, standard deviation (SD), tests of significance and 95% confidence interval (CI) were calculated. Gender difference between the two groups was analysed using chi square test. As the data was non-uniformly distributed, non-parametric test (Mann-Whitney) test of significance was used. Thus, inter-group comparison of mean differences in FVC, FEV1, FEF25-75, PEF, MVV was done by using Mann-Whitney test. P < 0.05 was considered statistically significant.

RESULTS

There was no significant difference in age, gender or

BMI in between the two groups viz. the adolescent sickle cell patient group (Cases) and the healthy control group (Control) as is depicted in table no. 1 and table no. 2. The pulmonary function test parameters and the type of spirometric abnormality are shown in table no. 3 and table no. 4 respectively. 22 (73.4%) had abnormal spirometric results, 18 (60%) had possible restrictive pattern, 2(6.6%) had obstructive pattern, 2(6.6%) had mixed pattern and 8 (26.6%) had no abnormality. Thus, the most common type of spirometric abnormality was a possible restrictive pattern. Table no. 5 represents the severity of spirometric abnormality which shows the spirometric abnormality in most of the cases to be of moderate severity.

Table 1: Age and BMI in adolescent SCA patients and healthy controls

Variables	Cases (SCA patients)	Control	p-Value
	Mean ± SD	Mean ± SD	
Age	14.933±3.321	15.1±2.440	0.8579
BMI	17.032±3.427	18.885±4.917	0.4463

Table 2: Gender wise distribution between adolescent SCA patients and healthy controls

Gender	Cases (SCA patients)	Control	Total
Male	17 (28)	17 (28)	34 (57)
Female	13 (22)	13 (22)	26 (43)
Total	30 (50)	30 (30)	60 (100)

Figure in the bracket indicate percentage.
Chi square =0.0000 p=1 df=1

DISCUSSION

The present study was designed to compare the pulmonary functions in adolescents with SCA with age, gender, and BMI matched healthy individuals. A total of 60 subjects i.e. 30 adolescent healthy individuals and 30 adolescents with SCA (HbSS) participated in the study. In our study, there were 17 males and 13 females in both cases and control group. Demographic details of the subjects in both groups (age, gender and BMI) were matching at baseline hence both the group were comparable. The study analysed the pulmonary functions in adolescent SCA patients and in normal healthy adolescent individuals.

Table 3: Pulmonary function analysis of adolescent SCA patients and healthy controls

Variables % predicted	Cases		Control		p-Value
	Mean ± SD	95% C.I.	Mean ± SD	95%C.I	
FEV1 (Forced Expiratory Volume in 1st Second)	73.1 ± 20.9	65.3-80.9	99.1 ± 18.5	92.2-106.0	<0.0001
FVC (Forced Vital Capacity	75.9 ± 20.0	68.4-83.4	96.4 ± 17.1	90-102.8	<0.0001
FEF25-75%(forced expiratory flow 25-75%)	66.9 ±30.7	55.4-78.4	94.5 ± 21.2	86.6-102.4	0.0007
PEF%	66.4 ± 14.1	61.1-71.7	85.7 ± 12.2	81.2-90.3	<0.0001
MVV%	71.0 ± 20.4	63.4-78.7	93.0 ± 12.4	88.3-97.6	<0.0001

Table 4: Type of Spirometry abnormality based on FEV1/FVC ratio between cases and control

Variables	Cases (%)	Control (%)
Obstructive	2 (6.6)	-
Restrictive	18 (60.0)	2 (6.6)
Mixed	2 (6.6)	-
No Abnormality	8 (26.6)	28 (93.3)
Total	**30 (100)**	**30 (100)**

Table 5: Severity of Spirometry abnormalities based on FEV1 in cases and control

Spirometry abnormality	Control (%)	Cases (%)
No Spirometry abnormality	28 (93.3)	8 (26.7)
Spirometry abnormality as per severity of FEV1		
>70%(mild)	2 (6.7)	4 (13.3)
60-69(moderate)	0	12 (40.0)
50-59(moderate-severe)	0	4 (13.3)
35-49(severe)	0	2 (6.7)
<35(very severe)	0	0
Total	**30 (100)**	**30 (100)**

Pulmonary functions (FVC, FEV1, FEF25-75, PEF& MVV) were statistically significantly decreased in cases as compared with control group.

The findings of the present study suggest that a possible restrictive pattern is the most common spirometric abnormality in patients with SCA.

Table no. 6 shows the major studies on patients with SCA published till date, most of which are in concordance with the findings of the present study depicting restrictive pattern as the predominant spirometric abnormality in these patients.

The probable reason of a possible spirometric restrictive pattern in patients with SCA may be related to peripheral vaso-occlusion, prior rib infraction or vertebral disease causing ineffective inspiration due to chest pain. Also, chest wall discomfort during testing which may be due to vaso-occlusion could lead to a possible restrictive abnormality on spirometry[7]. Bone infract, osteoporosis or osteomalacia in the vertebra causing structural impairments may lead to restrictive pattern[20]. The possible reason for a restrictive ventilatory disorder in these patients is the pulmonary infarction possibly due to vaso-occlusion and fat pulmonary embolism, which may be followed by an event like bone ischemia, with consequent replacement of lung parenchyma with fibrotic tissue.[21]

Two markers of the disease severity i.e. haemolysis and leucocytosis were related to decline in lung volume.[10] Higher leucocyte counts have been an independent risk factor for lower total lung capacity and vital capacity. Adherence of leucocytes to the blood vessel wall results in obstruction of lumen. They also stimulate the vascular endothelium resulting inexpression of ligands for adhesion. This leads to a cascade of events leading to tissue damage, and an inflammatory reaction resulting in further obstruction of capillaries and post capillary venules and thus resulting in a possible restrictive pattern.[10]

Lower lung volumes have also been shown to correlate with markers of chronic hemolysis (lower hemoglobin (Hb), higher baseline reticulocyte count or lactate dehydrogenase (LDH) value). Higher C-reactive proteins (CRP) levels suggestive of chronic inflammation are seen in subjects with lower Hb level, thus possibly playing a role in pathophysiology of the restrictive lung disease.[15]

Functional and structural impairments of pulmonary vessels have been seen due to endothelial dysfunction as a result of impaired arginine-nitric oxide pathway, oxidative stress and tissue damage. Also, interstitial pulmonary fibrosis may be present in transfused SCD patient having iron overload. Abnormal PFT may be due to excess production of proline, polyamines and dysregulated arginine metabolism. High levels of proline and arginase have been shown to have a role in the pathogenesis of pulmonary fibrosis in SCD patients.[22]

Thus, the result of the present study supports the hypothesis that there is significant difference in PFT parameters in adolescent SCA as compared to normal subjects and probability of restrictive ventilator defect in SCA patients.

The limitations of our study are as follows: 1. Symptomatic profile of the patients were not recorded in the current study and hence a correlation of the restrictive spirometric abnormality with a clinical parameter like the number of episodes of acute chest syndrome could not be arrived at. 2. Due to the resource limited settings, whole body Plethysmography and diffusion studies could not be done to confirm the restrictive spirometric abnormality. 3. Bronchodilator reversibility testing to assess airway hyperresponsiveness was not done in the current study.

CONCLUSION

Adolescent SCA patients have reduced pulmonary function test parameters signifying a possible restrictive ventilatory defect and hence pulmonary function assessment is of essentially important in these patients. However, PFT is a physiological test & should be correlated with other tests to confirm the structural abnormalities in patients with SCA. Considering the results of the present study, further studies on comparison of pulmonary functions in various age groups in SCA patients in Indian setup could yield valuable information. Also, future studies correlating pulmonary functions abnormalities with hematological investigations in SCA patients could provide another useful dimension to the possible etiology of restrictive spirometric abnormality.

Table 6: Various studies to assess the pulmonary functions in patients with Sickle Cell Anaemia/ Sickle Cell Disease (SCA/SCD)

Author name	Year /Type of study	Age group studied	Parameters	Results (Type of Spirometry abnormalities)
Present study	2012 Case control	10-19 yrs.	FEV1, FVC, FEF25-75, PEF, MVV	Restrictive predominant
Sylvester K.P et al [9]	2003 case control	64 children with SCD aged 5–16 years and 64 ethnic matched controls were re-cruited	Functional residual capacity using a helium gas dilution technique (FRCHe) and by whole body ple-thysmography (FRCpleth). Total lung capacity (TLCpleth), vital capacity (VCpleth), and residual volume (RVpleth) were also measured by whole body ple-thysmography, FEV1, FVC, FEV1/FVC, and PEF	Restrictive pattern.
Fonseca CSV et al [21]	2009 Cross sectional	50 SCD patients in the age 10 yrs. and above	FEV1, FVC, FEF 25-75%, (pre & post bronchodilator)	predominant Mixed respiratory pattern or combined type, fol-lowed by the classical restric-tive pattern
Tassel C et al [10]	2010 Co-hort Study	Children who were diag-nosed as SCA.	VC, FEVI, FRC, FEV1/FVC TLC, DLCO.	Restrictive pattern was pre-dominant.
Ezzat DA et al [11]	2009 obser-vational study	26 paediatric patients with 16 patients with â-Thalassemia & 10 patients with SCD	FVC, FEV1, FEV1/FVC%, FEF 25-75, FEF75, PEF), end systolic diameter, end diastolic diameter, Fractional shortening (FS%), Ejection Fraction (EF%), E/A ratio, Right Ventricular Diameter (RVD) & pulmonary artery sys-tolic pressure (PASP)	PFT reflecting restrictive lung abnormalities. And pulmonary hypertension in â- thalassemia &SCD start early in childhood
Hagag AA et al [12]	2014 case control	40 children with SCA age ranging from 7– 15 years	FEV1, FEV1% FEV1/ FVC ra-tio, PEFR, PEFR% FEF, FVC, FVC% serum ferritin, serum iron and Total iron binding capacity (TIBC), complete blood count (CBC)	In the present work, there were restrictive spirometric pattern in 75% of studied pa-tients with sickle cell anaemia and mixed obstructive and re-strictive pattern in 25% of pa-tients
Oko-Ose JN et al [4]	2012 Case control	60 subjects (30 patients and 30 control groups)	FVC, FEV1, and FEV1/FVC FVC%, FEV1%, and FEV1/FVC% predicted	The lung function declined with age. This work has also shown that the most common pulmonary function test (PFT) abnormality was restrictive dis-ease pattern (76.7%)
Cook J et al [13]	2013 Cross Sectional	25 children aged 7-16 yrs. with electrophoretically confirmed SCD	FEV1, FVC and FEV1/FVC ra-tio	spirometric abnormalities sug-gestive of restrictive lung dis-ease with no evidence of ob-structive defects
MacLean JE et al [14]	2008 Longi-tudinal Study	413 children SCD in the age group of 8-18 yrs. -	FEV1, FVC, FEV1/FVC FEF25–75, TLC, and RV.	Restrictive defect. the decline begins in childhood
Williams K et al [15]	2012 Case control	74 controls and 154 SCD subjects with mean age 31yrs.	FVC, FEV1, FEV1/FVC FVC%, FEV%1, and FEV1/FVC%	sickle cell disease tends to have lower lung function parameters than healthy controls con-sistent with a restrictive defect
Klings ES et al [16]	2006 Cross Sectional	310 adults with Hb-SS were analysed	FEV1, FVC, FEV1/FVC, TLC, RV, and Diffusing lung capacity for Carbon monoxide (DLCO)	Pulmonary functions are ab-normal in 90% of adult with Hb-SS. and Restrictive physi-ology and decreased DLCO.
Molavi MA et al [17]	2011 Cross Sectional	29 subjects (SCA with Acute Chest Syndrome) in the age group of 6-18 years,	FEVI/FVC.	Pulmonary functions abnormal in 79.3% and restrictive pat-tern, normal pattern (20.7%, 6 cases) and obstructive pattern (6.9%, 2 cases).

Author name	Year /Type of study	Age group studied	Parameters	Results (Type of Spirometry abnormalities)
Hulke SM et al[7]	2011 Cross sectional	20-40 yrs. 133 subjects (SCD)	FEVI/FVC, FVC, FEVI, PEFR, MVV, FEF25-75%, FEF50%, FEF75%.	Restrictive pattern.
Santoli F et al[18]	1998 Cross Sectional	49 subjects (SCD) in the age group of 16–49 yrs.	TLC % pred, FVC % pred, FRC % pred, FEV1 % pred, FEV1/VC %, pred FEF50 % pred, FEF25 % pred, FEF25–75 % pred, (Respiratory resistance) Rrs, KCO % pred TLCO %	Obstructive pattern
Fawibe AE et al [19]	2006 case control	57 SCA were compared with 60 age matched control. The age of patients was in between 18-32 yrs. and of control was between 17-30 yrs.	FVC, FEV1, PEFR	Restrictive pattern predominant.

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ORIGINAL ARTICLE

ANALYSIS OF SERUM ANGIOTENSIN CONVERTING ENZYME (ACE) ACTIVITY ACROSS ACE GENOTPYE IN NEWLY DIAGNOSED HYPERTENSIVE PATIENTS

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ABSTRACT

Introduction: Essential hypertension is a multifactorial disease in which genetic and environmental factors play an important role. Angiotensin-I converting enzyme is a core enzyme of renin-angiotensin system and is known to play a critical role in the homeostasis of blood pressure. **Aims:** To determine the association of the serum ACE activity with regard to ACE insertion/deletion polymorphism with essential hypertension in the adult Gujarati hypertensive patient.

Research design and methods: A cross-sectional study was conducted with 173 patients with essential hypertension and 186 controls were recruited for the study. DNA samples were isolated from peripheral blood. Polymerase chain reaction was used for genotyping and ACE activity and other biochemical variables were measured.

Result: Genotype distribution in patients and controls were significantly different. Albeit the genotype frequency resulted in a higher frequency of the D allele in the group of cases than controls, the difference in allele frequency did not reach statistical significance and a trend of increase in SBP, DBP and serum ACE activity with increasing number of D alleles was observed..

Conclusion: Serum ACE activity and ACE I/D polymorphism plays a significant role in the pathogenesis of hypertension.

Keywords: Angiotensin converting enzyme, ACE activity, Essential hypertension

INTRODUCTION

Essential hypertension affects approximately 20% of the adult population and is one of the contributing factors for the onset of macrovascular complications.[1] Its pathogenesis involves interactions between genetic and environmental factors, with approximately 30% of the inter-individual variability in blood pressure being genetically determined.[2] The exact etiology of this disease is still unknown, but special attention has been given to renin–angiotensin system (RAS), due of its physiological magnitude in cardiovascular homeostasis and the genes that regulate the system may contribute to the development of hypertension and end-organ damage.[3] Angiotensin converting enzyme (ACE) is a core enzyme of the RAS, and a possible candidate gene.

ACE converts inactive angiotensin I into active angiotensin II, which is a peptide with multiple functions, including vasoconstriction, aldosterone production, and noradrenaline release from sympathetic nerve endings. It has hypertropic and hyperplastic effects on vascular smooth muscle and cardiomyocytes, synthesis of the extracellular collagen matrix, and is tightly intertwined with the cascade of inflammatory, thrombotic, and fibrotic factors.[4]

The ACE gene is located at 17q23 and contains a polymorphism distinguished by either an insertion (I) or deletion (D) of a 287 base pair segment in intron 16.[5] The ACE DD genotype has been associated with higher levels of ACE[6], BP[7], and increased cardiovascular risk.[6] Despite the degree of interest shown in the subject, relatively few studies have examined the ACE enzyme activity in essential hypertensive patients with respect to I/D polymorphism, particularly in Gujarati population. Thus, in present study an attempt has been made to explore the association of the serum ACE activity with regard to ACE insertion/deletion polymorphism with essential hypertension in the adult Gujarati hypertensive patient.

METHODOLOGY

This study was designed to determine the serum ACE activity with regard to ACE I/D polymorphism in newly diagnosed hypertensive patients. 359 participants were enrolled from November 2015 to April 2017 on the basis of consecutive sampling technique and were categorized into two main groups which include:

Group I : Healthy controls i.e. subjects not suffering from diabetes, nor having any family history of diabetes, not suffering from hypertension or from any acute or chronic disease , nor taking any drugs believed to alter blood pressure; n = 186

Group II : Hypertensive patients [Based on the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VII)[8]; n = 173

Exclusion criteria were:

- Patients who needed continuous or periodic use of corticosteroids.
- Patients who visited the pregnancy clinic or who had given birth within the preceding six weeks.
- Patients taking blood pressure and or lipid lowering drugs.
- Lack of approval by physician for any reason(s).
- Subjects showing disinterest.

All subjects were studied as outpatient. Participant's examination included interviews for medical and nutritional history. Present and past history of each case was recorded in detail regarding their general information i.e. name, age, sex, address, religion, occupation, economic status, nutritional and personal habits, education, medication and history suggestive of any systemic illness. Each subject was then examined for various anthropometric parameters: Weight (Kg) and height (meters) were measured. Body Mass Index (BMI) was calculated by Weight (Kg) / height squared (m²). Waist circumference was assessed in the standing position, midway between the highest point of the iliac crest and the lowest point of the costal margin in the mid-axillary line. Hip circumference was measured at the level of the femoral greater trochanter. All anthropomorphic measures reflect the average of 2 measurements. Blood pressure (BP) was measured in the seated position after 10 minutes of rest with a standard manual mercury sphygmomanometer. Subjects were diagnosed by physician with hypertension on the basis of JNC-7. Age was defined as the age at the time of interview.

After an overnight fast of 12 hours, venous sampling was done for biochemical determinations and for isolation of DNA. Serum and plasma was separated by centrifugation of blood sample and were subjected for analytical procedures. Glucose (Glucose oxidase method, CV %: 3.4), cholesterol (Cholesterol oxidase method, CV %: 3.9), triglycerides (Enzymatic method, CV %: 3.6), HDL-C (Phosphpotungstic method, CV %: 4.7), creatinine (modified Jaffe's method, CV % 4.1) and angiotensin converting enzyme activity by Cushman and Cheung method , modified by Letreut et al (1979) were measured. LDL and VLDL cholesterol were calculated. Genomic DNA was extracted from peripheral blood leukocytes using commercially available DNA extraction and purification kit based on standard proteinase K technique.

Two oligonucleotide primers, forward: 5'-CTG GAG ACC ACT CCC ATC CTT TCT T-3' and reverse: 5'-GAT GTG GCC ATC ACA TTC GTC AGA T-3'based on the flanking sequences of the I/D region on the intron 16 of ACE gene were used to amplify the corresponding DNA fragments by polymerase chain reaction (PCR). Amplification was carried out in a DNA Thermal Cycler in a final reaction volume of 50 µl containing 50ng genomic DNA, 20pM each primer, 2.5mM each deoxyribonucleotides triphosphate, 1U thermus aquaticus DNA polymerase, 1.5mM magnesium chloride, amplification buffer contained 20mM Tris-hydrocholric acid and 50mM KCl. The thermocycling profile consisted of one minutes of initial denaturation at 94°C followed by 30 cycles of amplification of denaturation at 95°C for 30 sec, annealing at 58°C for 1 min and extension at 72°C for 2 min, followed by a final extension at 72°C for 5 min. Using agarose gel (1%) electrophoresis, amplified products were separated and distinguished using ethidium bromide under UV light as a 190 bp fragment in the absence of an Alu repeat insertion and a 490 bp fragment in the presence of the insertion (genotypes described as II-490 bp, ID-490+190 bp, and DD-190 bp). These experiments were approved by Institutional Ethical Committee.

Statistical analysis: Data analyses were performed with the SPSS 15.0 statistical software. The results for continuous variables are mean $\pm$ SD and are well within the normal curve (i.e. normality is maintained). The two tailed (unpaired) student's test for independent samples, analysis of variance (ANOVA) was used, in assessment of the significance of difference between group means. The distribution of alleles in studied groups was tested for fitting to the Hardy–Weinberg equilibrium (HWE) (using web base program: http://www.oege.org/software/hwe-mr-calc.shtml) through testing the difference between observed and expected frequencies of genetic variants using the $\chi 2$ goodness-of-fit test. For all analyses, the nominal level of statistical significance was<0.05.

RESULTS

Table 1 shows the subgroup, anthropometric and clinical characteristics of the study participants.

Among the study participants there was a predominance of male individuals as compared with females (p<0.05) but mean age of hypertensive participants and controls were similar. A comparison of different variables revealed that the difference were statically significant between cases and controls with respect to glucose, BMI, lipid profile (higher levels of total cholesterol, TG and lower levels of HDL-C) along with higher systolic blood pressure (SBP) readings and diastolic pressure (p<0.05; Table 1).

Genotype distribution in patients and controls were significantly different. The difference was due to sig-nificantly higher frequency of ACE DD homozygotes, and lower frequency of heterozygote ACE ID (Table 2).

Albeit the genotype frequency resulted in a higher frequency of the D allele in the group of cases than controls, the difference in allele frequency did not reach statistical significance with this sample size. Testing genetic equilibrium between the observed and expected genotypes using HWE showed ACE genetic variants were confirming to the law in all groups (Table 2).

Table 1: Characteristics of study population

Parameters	Group I; Control (n:186) Mean ± SD	Group II; Hypertensive (N:173) Mean ± SD
Age	49.3 ± 10.3	50.7 ± 11.4
Males [n (%)]	102(54.83%)	108 (62.42%)*
BMI (kg/m²)	22.7 ± 4.3	26.4 ± 5.7*
Waist/hip ratio	0.91 ± 0.05	0.95 ± 0.06*
Systolic BP (mmHg)	126 ± 10	144 ± 22*
Diastolic BP (mmHg)	80 ± 8	88 ± 10*
Fasting plasma glucose (mg/dl)	77.8 ± 11.3	91.4 ± 9.8*
Triglycerides (mg/dl)	119.6 ± 21.8	161.7 ± 29.2*
Total cholesterol (mg/dl)	162.5 ± 25.6	198.5 ± 44.3*
HDL- cholesterol (mg/dl)	48.5 ± 6.4	43.5 ± 4.4*
LDL- cholesterol (mg/dl)	87.9 ± 20.4	123.2 ± 31.2*
VLDL- cholesterol (mg/dl)	25.4 ± 8.6	35.6 ± 9.8 *
Serum ACE (SACE) (U/L)	17.46 ± 2.41	40.80 ± 3.96*

*p-Value<0.05 (Group II Vs Group I)

Table 2: Genotype distribution and allele frequencies of ACE I/D polymorphism in Hypertensive patients and in controls.

Genotypes	Control (n=186)	Cases (n=173)	p-Value	OR (CI)
ID	109 (58.6%)	63 (36.41%)	0.008	0.42 (0.22 – 0.80)
DD	40 (21.5%)	75 (43.35%)	0.007	2.60 (1.31 – 5.18)
HWE: x^2; p-Value	2.30; 0.13	3.63; 0.06		
p allele (I) frequency	0.49	0.39		
q allele (D) frequency	0.51	0.61		

Table 3: Clinical characteristics and biochemical variables of hypertensive patients across ACE genotype

Characteristics	II (n=35)	ID (n=63)	DD (n=75)
Age	51.4 ± 9.2	48.6 ± 10.2	51.2 ± 8.6
Males [n (%)]	22(62.85%)	41 (65.07%)	45 (60.0%)
BMI (kg/m²)	26.6 ± 5.8	26.8 ± 4.8	25.9 ± 5.6
Waist/hip ratio	0.96 ± 0.04	0.94 ± 0.08	0.95 ± 0.04
Systolic BP (mmHg)	140 ± 18*	146 ± 24*	148 ± 20*
Diastolic BP (mmHg)	84 ± 12*	88 ± 8*	90 ± 8*
Fasting plasma glucose (mg/dl)	90.2 ± 10.4	94.6 ± 8.8	92.0 ± 6.6
Triglycerides (mg/dl)	158.7 ± 25.6	160.7 ± 30.4	164.8 ± 28.6
Total cholesterol (mg/dl)	196.5 ± 48.2	201.6 ± 42.6	197.3 ± 40.5
HDL- cholesterol (mg/dl)	43.6 ± 4.8	42.9 ± 4.7	43.8 ± 4.1
LDL- cholesterol (mg/dl)	121.2 ± 28.4	125.4 ± 32.1	123.7 ± 29.8
VLDL- cholesterol (mg/dl)	33.9 ± 9.1	36.1 ± 10.2	36.6 ± 8.4
Serum ACE(SACE) (U/L)	34.4 ± 4.1*	42.8 ± 3.4*	48.6 ± 3.2*

*p-Value<0.05

Table 4: Multivariate logistic regression analysis

Genotype	Control	Cases	OR (CI)
Serum ACE activity (U/L)			
II	14.2 ± 2.2	34.4 ± 4.1	1.0
ID	16.1 ± 2.6	42.8 ± 3.4	1.2 (1.04-1.97)
DD	22.1 ± 2.1	48.6 ± 3.2	1.8 (1.08-3.74)

The comparison of blood pressure levels and other variables across ACE genotype showed that there was a trend of increase in SBP, DBP and serum ACE activity with increasing number of D alleles (Table 3). However, neither serum ACE concentrations nor BP values differ significantly between men and women and were not correlated to age and BMI. Table 4 provides the serum ACE activity according to variant form of ACE polymorphism, with activity of 34.4 ± 4.1, 42.8 ± 3.4 and 48.6 ± 3.2 U/L in II, ID and DD genotyped hypertensive patients respectively.

DISCUSSION

Association between ACE levels, ACE polymorphism and essential hypertension, is controversial. In different studies[9,10] no strong correlation has been found between plasma ACE levels and hypertension or between ACE polymorphisms and hypertension. Even in experimental study carried out by Kessler et al[11], with transgenic mice, suggest that serum ACE level is not enough to maintain blood pressure normal and that endothelial cell-bound ACE is critically important for maintaining blood pressure. On the contrary, other studies have suggested that the plasma ACE activity is higher in adults with essential hypertension.[12,13] In children, ACE has been found to be positively associated with blood pressure levels and contribute to the development of hypertension.[14] We therefore considered it worthwhile to unravel the serum ACE activity in relation to I/D polymorphism in newly diagnosed adult hypertensive patients with respect to disease and indeed found a significant interaction with the disease phenotype.

Result presented here supports to the hypothesis that ACE activity and hypertension are associated. The primary finding from this study using a case control approach, involving individuals with newly diagnosed EHT is that ACE activities were highest in DD carriers, then in II carriers, and intermediate in ID carriers. Multivariate meta-analysis after adjustment for the covariates, did not change the significance of the results. (p<0.05, 95% CI 1.08 – 3.74, Table 4), implying a risk of approximately 1.8 times higher than for those homozygous for the I allele. This result was consistent with the studies that reported that ACE activities were significantly higher in patients with DD genotype versus the two other groups having ID and II genotype.[6,15,16] However, Ljungberg's[17] report-ed that individuals with the II group had considerably higher plasma ACE level than most DD carriers.

We also analyzed the genotypic and the allelic distributions of the ACE I/D polymorphism between controls and hypertensive patients. Genotype data were available for all participants, frequency of DD genotype was found to be significantly higher in cases than in control participants (p<0.05). Therefore, we suggest that the genetic variation at the ACE locus as DD variant in intron 16, contribute to an increased risk of hypertension. Our findings were in conformity with other studies[18,19] but not all.[20] This difference may possibly be due to different races, methods of quantitation and patient selection.

In conclusion, serum ACE activity and ACE I/D polymorphism revealed significant influence on hypertension. However, limited information on potential risk factors may restrict the ability to make a detailed confounding adjustment for all factors essential for the study of hypertension. Therefore, the relationship between the ACE I/D polymorphism and serum ACE activity, with EH is still inconclusive, large scale studies with different ethnicities are warranted.

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ORIGINAL ARTICLE

PAEDIATRIC LOW VISION: MAGNITUDE, INTERVENTIONS, DETERMINANTS AND COMPLIANCE

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ABSTRACT

Aim: To assess the low vision problem and its management along with impact assessment in paediatric population (children aged 0-16 years from blind schools and paediatric patients visiting the low vision department of a tertiary eye care centre).

Materials and Methods: In this cross-sectional study in which out of the total 3463 children from both the groups, 314 from blind schools and the 3149 from tertiary eye care centre in Pune a total of 113 children with low vision were assessed between October 1st 2007 and October 1st 2008. A complete low vision examination was done and appropriate aids were provided. Two follow up examinations were done at 3 and 9 months. Demographic information and entire assessment was done as per the modified WHO/PBL form for blind with low vision assessment and a questionnaire to assess the compliance.

Results: Out of 314 children from the schools for blind, 19.10%(60 number) were found to have low vision, majority having globe anomaly as the determinant and out of 3149 in the tertiary eye care centre 1.68% (53) were found to have low vision, majority with retinal lesions. All the children with vision <6/60 showed significant improvement in vision. In schools for blind, out of 52 who had vision <6/24, 35 (58.33%) improved to >6/24 range. In tertiary eye care centre, out of 49 who had vision <6/24, 24 (45.28%) improved to >6/24 range. After correction 61.7% in blind schools and 67.9% in the tertiary eye care centre had their near vision improved to the range of 1.5M – 1M.

Conclusions: Good screening, assessment and early management of low vision in children is important so as to help them become independent citizens and reduce the load of visual impairment.

Keywords: Low vision, Screening, Vision 2020

INTRODUCTION

The World Health Organization estimates 161 million people worldwide have a visual impairment. Of these, 37 million are blind and 124 million have low vision (World Health Organization, 2000). More than 90% of worlds visually impaired live in developing countries like India. The working definition of low vision used will be as given by WHO in 1992 i.e. – A person with low vision is one who has impairment of visual functioning even after treatment and/or standard refractive correction, and has a visual acuity of less than 6/18 to light perception , or a visual field of less than 10 degrees from the point of fixation ,but who uses ,or is potentially able to use vision for the planning and /or execution of the task for which vision is essential.[1] The problem of low vision has come in limelight at international level attracting attention of the global initiative VISION 2020: The Right to Sight. About 90% of the world's blind live in the developing world. It is estimated that there are 9-12 million blind in India, which amounts to about one-fourth of all the blind people worldwide. More than 12 million children aged 5 – 15 years worldwide are visually impaired. This study is an attempt to reach out to screen and treat children with low vision so as to help them use their residual potential vision to the best and lead a better quality life.

METHODOLOGY

This is a cross-sectional study wherein comprehensive data was collected from children aged 0-16 years, attending schools for blind in and around Pune and those with low vision examined in a tertiary eye care centre, between November 1st 2007 and September 1st 2008. Entire examination was done by a team of

ophthalmologists, low vision specialist, optometrist and retina specialist. Data collected comprises clinical and demographic details and educational status. Case record includes a special modified version of WHO/PBL eye examination record for children with blindness; including entire low vision assessment. Complete visual assessment was done. Dry retinoscopy was done and whenever needed radical retinoscopy at reduced working distance / wet retinoscopy were performed. Visual acuity was tested using the Lea symbol charts for near and distance. Contrast sensitivity was assessed using Hand Held Low Contrast Flip Chart with Lea symbols. Contrast sensitivity measures the ability to see details at low contrast levels. The decision of prescribing a monocular or binocular aid was taken first depending on the results of acuity and contrast testing and also considering the difference between the two eyes along with the binocular interactions. Anterior segments of the eyes were examined using a torch and / or handheld slit lamp. The posterior segment was examined using a direct ophthalmoscope and indirect ophthalmoscope after dilatation of pupil.

The amount of magnification needed was determined by the following formula:

Magnification = Best visual acuity / Target acuity

For near: Kestenbaum method was used. Appropriate spectacle and low vision aid (optical and/or non optical) were provided based on the needs with specific training to use them. Compliance was checked by observation in the follow up (whether child was wearing/using the aid or not) and by verbal questions regarding the reason for not using the aid. Assessment of outdoor and indoor activities was done by means of leading questions related to mobility, recognition of faces and objects, own daily routine work, playing, art work (cane work) was also done. The quality of life was assessed on the basis of the changes noticed in mobility, recognition and other outdoor, routine and vocational activities.

Two follow up examinations were done at three months and nine months respectively from the first examination.

Permission was obtained from ethical committee of the institutional to conduct the study. Informed written consent of the participants was taken. The data was entered into a database and analyzed using SPSS (statistical package for social sciences), version 16.0 statistical software for Windows. Chi square test and t test was applied wherever applicable.

RESULTS

In the schools for blind out of 314 children 60(19.1%) children and in the tertiary eye care centre out of 3149 children attending the pediatric OPD

oven 1 year period, 53(1.7%) were found to have low vision. (Table1)

Majority of children from the schools for blind, i.e. 51.7%, had whole globe anomalies like microphthalmos as the determinant of low vision followed by retinal causes like heredomacular degeneration etc (28.3%) and others. On the other hand, the majority of children from the tertiary eye care centre had retinal lesions as the determinant of low vision followed by whole globe anomalies. (Table 2)

All the children from schools for blind were given optical and non optical aids. Only 7.5% of children from tertiary eye care centre showed no improvement with aids tried.

Table 1: Sample population description

Type of population	Children examined	Children with low vision (%)
Blind schools	314	60 (19.10)
Tertiary eye care centre	3149	53 (1.68)
Total	3463	113

Table 2: Various determinants of low vision according to anatomical site involved

Determinant / diagnosis	Blind schools	Tertiary eye care centre (%)
Whole globe	31 (51.7)	14 (26.4)
Cornea	2 (3.3)	1 (1.9)
Lens	6 (10%)	0
Retina	17(28.3)	25 (47.2)
Optic nerve	1 (1.7)	6 (11.3)
Trauma	0	1 (1.9)
Amblyopia and refractive error	3 (5)	6 (11.3)

In the schools for blind, 16.7% children improved to the 6/18-6/9 range of distance vision. All the children with vision (less than) <6/60 showed improvement in vision. Out of 52 children who had vision <6/24, 35 (58.33%) improved to equal to or (more than) >6/24 range. This is statistically significant by t-test, p value <0.01. In the tertiary eye care centre, 15.1% children improved to the 6/18 - 6/9 range. 10 of 18 children i.e. 18.86% with vision <6/60 showed improvement in vision. Out of 49 who had vision <6/24, 24 (45.28%) improved to >6/24 rangewhich is statistically significant by t test with p value <0.05. (Table 3) After correction, 61.7% in blind schools and 67.9% in the tertiary eye care centre had their near vision improved to the range of 1.6M – 1M (N12-N8). This is statistically significant with p value <0.05 by t-test.

In schools for blind: Out of 60 who were given aids, only 8.3% broke their aids while 2 (3.3%) found it difficult to use the aid, 3 (5%) left the aid somewhere.

Table 3: Improvement in Distance vision & Near Vision Unaided

Vision	Blind School		Tertiary Eye Care Centre	
	Before correction (unaided)	After correction	Before correction (unaided)	After correction
Distance Vision				
< 6/60 – PL	21 (35.0)	0	18 (34)	8 (15.1)
6/60 -6/24p	31 (51.7)	17 (28.3)	31 (58.5)	17 (32.1)
6/24 - 6/18p	8 (13.3)	27 (45.0)	4 (7.5)	18 (34.0)
6/18 - 6/9	0	10 (16.7)	0	8 (15.1)
No Improvement		6 (10.0)		2 (3.77)
Near Vision Unaided				
< 8M	0	0	2 (3.77)	0
8M – 4M	24 (40)	8 (13.33)	13 (24.5)	14 (26.41)
3M – 2M	28 (46.7)	13 (21.7)	24 (45.3)	3 (5.7)
1.5M – 1M	8 (13.3)	37 (61.7)	14 (26.4)	36 (67.9)
No Improvement		2 (3.33)		0

This suggests that only 5 children were probably not very happy with the aid. In tertiary eye care centre: only 1.9% found it difficult to use the aid and another 1.9% broke the aid. 96.7% children from schools for blind and 92.5% from tertiary eye care centre were dependent in their mobility but with the use of aids provided 61.7% from the schools for blind and 52.8% from the tertiary eye care centre became independent. 58.3% children from schools for blind and 35.8% from tertiary eye care centre could comfortably play outdoors with the aids provided. 5% children from schools for blind and 7.5 % from the tertiary eye care centre could cross the roads independently with the aids provided. With regular use of aids: 35% children from schools for blind and 45.3% from the tertiary eye care centre learnt to read. 63.3% children from schools for blind and 50.9% from the tertiary eye care centre started to recognize faces and objects at 3m. 61.7% children from schools for blind and 41.5% from the tertiary eye care centre could wash and maintain their clothes better with the aids.

DISCUSSION

This study presents data on the magnitude, determinants and interventions in the sample population of children with low vision from schools for blind and a tertiary eye care centre. The distribution of the study population according to age showed that most of the patients of low vision were in the age group of 10 – 16 Years as compared to those in the age group less than 10 years. According to the study of Gilbert CE et al in school age children, functional low vision increased with age.[2] The various determinants of low vision in children seen in the schools for blind consisted mainly of whole globe problems (51.7 %) followed by retinal lesions (28.3 %), whereas in the tertiary eye care centre, it consisted of retinal lesions (47.2 %) followed by whole globe anomalies (26.4 %). Study of the temporal trends of severe visual impairment/Blindness by comparing causes in children in three different age groups-5-8 years, 9-12 years, and 13-16 years-suggests that retinal disorders have become more important. The whole globe (27.4%), cornea (21.7%), and retina (15.1%) were found to be the most frequent sites of abnormality. Congenital ocular anomalies (mainly microphthalmos, anophthalmos) accounted for 25.8% of severe visual impairment / Blindness. The retinal disorders being identified as important is in agreement with the results in our tertiary eye care center study group.Similar findings have been reported from other institution based and population based studies in India by Titiyal JS et al and Hornby S et al.[3,4] Congenital anomalies may be due to genetic diseases or intrauterine factors, but in the majority, the etiology is unknown. Similar results were seen in the study by R Sitorus et al in Indonesia where whole globe anomalies were the major determinant of low vision.[5] The most commonly given optical devices were distance correction spectacles (53.3 %) in schools for blind; 41.5 % in tertiary eye care center) and then, bifocals (12%) in schools for blinds. In the two study groups, 61.7 % and 67.9 % children respectively, could read 1.5 - 1M (N10 – N8) print. This was in agreement with the study of Pal N et al in which out of 124 children with low vision but having useful residual vision, 51 (41.1%) were able to read N-10 unaided or with distance spectacles and 30 children (22.6%) improved to N-10 with spectacle magnifiers and were prescribed the same.[6] Our study differed in that low vision children were not very happy with the improvement they gained with magnifiers as compared to other studies. Thus, it was observed that majority of children in blind schools (53.3%) and tertiary eye care centre (41.5%) accepted spectacles (distance correction) as optical aids. Results similar to our study were seen in the study of Silver J et al; forty six per cent of students with low vision (n = 64) could read N5-N8 print unaided or with spectacles, as could a further 33% (n = 46) with low vision de-

vices.[7] A study by Hornby SJ et al showed that 15.4% were able to read N10 point though they were studying Braille.[4] In our study only 7.5% children from the tertiary eye care centre showed significant improvement with telescopes which is quite less as compared to other studies like one from the blind schools of Nepal by Kansakar I et al.[8] The compliance in terms of follow up rate was good in 83.3% and 62.3% from the schools for blind and tertiary eye care center respectively. These children were not only present during the first follow up but 66.7 %; 58.5 % from the two groups respectively were also using the aids provided. This indicates the satisfaction and improvement in the quality of life of these children. Independence in mobility was seen in almost all the children using the aids regularly. Good improvement was observed in the outdoor and routine activities. Significant improvement in craft work was also noted. Similar results regarding satisfaction with low vision aids was seen in the study by Rohrschneider K et al.[9] As far as non optical devices were concerned, additional illumination in the form of overhead table lamp or window light was helpful in 80% and 79.2% children in the two study groups respectively, while a Reading stand was the preferred aid in 86.7% and 64.2% children respectively. In the second follow up, 51.7% children from the schools for blind and 66% children from the tertiary eye care center were found to be using the aids regularly. The lower percentage of children using aids in the blind schools probably indicates that over a longer period of time, more attention was paid to the children in the tertiary eye care center. This also implies that the needs of children in schools for blind may have been neglected by teachers/guardians ,whereas in the second group, it was the parents/close relatives who were taking care and were, therefore, more cautious.

Thus, Low vision/ "partial sight" can be managed well with low vision services thereby improving the quality of life of children with low vision. Thus, it is important to screen out patients of low vision from blind schools to provide them with appropriate aids.

More so in children as early management and provision of aids will help them cope with their daily needs, social and educational needs as well. This will enhance their performance in school and develop their self confidence. And help in their social acceptance and thus enlighten their dark world. Our study, thus, emphasizes on the great need of proper screening of children in blind schools and tertiary eyecare centres/clinics for low vision and appropriate management with refraction and low vision services.

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ORIGINAL ARTICLE

REGIONAL VARIATION OF MORPHOMETRIC MEASUREMENTS OF PROXIMAL END OF FEMUR IN COASTAL ANDHRA PRADESH AND ITS CLINICAL IMPLICATION TO IMPROVE SURGICAL OUTCOME

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ABSTRACT

Introduction: The neck of femur is an important modification in human being. The neck-shaft angle and different parameters of neck are clinically important to diagnose pathological conditions of the hip joint and also helpful in the treatment and follow-up of fractures around proximal end of femur. The present study is an attempt to evaluate the normal range of anterior and posterior neck length, diameter of head and neck of femur and cross sectional area of neck of adult femora and neck-shaft angle in South Indian Population.

Methodology: Adult femora available in the anatomy department of different Medical Colleges in coastal Andhra Pradesh were used as study sample to get exact idea of femoral morphometry. Goniometer and Vernier calliper were used to measure all the parameters. Values were analyzed by using statistical software (SPSS programmed, version-17)

Results: Analyzed value of present study regarding neck-shaft angle, neck length, diameter of neck, diameter of head and cross sectional area are 126^0, 29.5mm & 31.6mm, 23.6mm, 43.1 mm and 437.21mm^2 respectively.

Conclusion: The results of present study might be helpful for bio mechanical engineer to design implant specific for South Indian population.

Keywords: Morphometric Measurement, Cross Sectional Area, Hip Replacement Therapy, Prosthesis

INTRODUCTION

The Femur or thighbone is the longest and strongest bone of human body. The proximal end of femur comprises of the head, neck, two trochanters and adjacent structures. The neck of femur is an important modification in human being. The femoral neck is approximately 5cm long and connects the head to the shaft at an average angle of 125 degree.[1] Not only the neck-shaft angle facilitates movement at the hip joint but the femoral neck also provides a lever for the muscles acting around the hip joint. The neck-shaft angle, diameter of head and neck, anterior and posterior neck length and cross sectional area of the neck of the femur are clinically important parameters to diagnose pathological conditions of the hip joint and also helpful in the treatment and follow-up of fractures around proximal end of femur. The neck is the weakest part of the femur and the fractures are mostly intra-capsular[2] in type and they form a major subtype of fractures around the proximal end of femur. The treatment may be non-operative management or internal fixation or prosthetic replacement. Standard implants are mostly used to treat fractures of neck and head of femur. If the sizes of implants are not appropriate there may be pain and other complications.[3] To minimize these complications the knowledge of the normal anatomical values of proximal end of femur is required. These normal values may vary in different age group. More over racial variations are also observed. The present study is an attempt to evaluate the normal range of anterior and posterior neck length and cross sectional area of neck of adult femora in South Indian Population and to compare it with the other races like Caucasian, Negroes etc as stated in different literatures that might be helpful for orthopedic surgeon in case of internal fixation and hip replacement therapy.

METHODOLOGY

Goniometer and Vernier calipers were used to measure all the parameters. Values were analyzed by using

statistical software (SPSS programmed, version-17). The present study was done on adult femora available in the Anatomy department of different medical colleges in coastal Andhra Pradesh for a time period of one year (2012-2013). It was a descriptive, cross sectional type of study. Written permission from the competent authorities was obtained for inclusion of femora from different institutions. All together 220 adult femora were final sample size for the study. Only intact adult femora were taken after the determination of side. **Exclusion criteria:-**Young bones where epiphysis and diaphysis are not united**,** deformed bone or femur with marks of old fracture**,** any bones having marks of decay were excluded from this study**,** sex determination were excluded from the study. The anterior and posterior neck length were measured along long axis of the neck both anteriorly and posteriorly using Vernier calipers. For anterior neck length (ANL), a mid- point was determined on inter-trochanteric line and point on base of head of femur and then distance between two points were measured by using Vernier calipers [Fig.1]. Similarly posterior neck length (PNL) was measured on posterior aspect of neck. Diameter of neck (DON) was measured using Vernier calipers at the narrowest part of the neck [Fig. 2].The diameter of head (DOH) was measured using Vernier calipers at the widest part of head [Fig. 3]. Neck shaft angle was measured by using goniometer [fig. 4].

RESULTS

It is seen from analysis of tabular values that computation of 220 ungrouped data irrespective of side gives average value (mean) of neck-shaft angle as 126.65^0. Corresponding standard deviation and standard error are 5.92and 0.40 respectively. The average value (mean) with standard error of anterior neck length, posterior neck length, diameter of neck and transverse diameter of head are 2.95+/-0.04 cm, 3.16+/-0.04 cm, 2.36+/-0.03 cm and 4+/-0.03 cm respectively. Standard deviation for above mentioned cases is 0.53, 0.58, 0.47 and 0.52 respectively (Table 1).

Figure 1: Picture showing how to measure Anterior Neck Length (ANL)

Figure 3: Method of measurement of diameter of head

Figure 2: Measurement of diameter of neck by using Vernier caliper

Figure 4: Picture showing the measurement of neck-shaft angle by Goniometer

Table 1: Measurements of Various Parameters of Dry Adult Femora (n-220)

Parameters	Mean	Std. Deviation	Std. Error of mean
Neck–shaft angle (deg)	126.65	5.92	0.40
Anterior neck length(Cm)	2.95	0.53	0.04
Posterior neck length(Cm)	3.16	0.58	0.04
Diameter of neck(Cm)	2.36	0.47	0.03
Transverse diameter of head(Cm)	4	0.52	0.03

DISCUSSION

The proximal end of femur has been the subject of much attention for orthopaedic surgeons as operation on proximal end of femur is one of commonest site in orthopaedic surgical practice and main aim of this operation is to remove pathology and restore normal anatomy as far as possible.[4] Properly selected and implanted total hip components of most designs can be expected to yield satisfactory results in a high percentage of patients. No implant design of the system is appropriate for every patients, and a general knowledge of the variety of component designs and their strengths and weaknesses is an asset to the surgeon. Selection of implants is not only based on the patient's needs, and level of activity along with the bone quality but, also depends on dimensions of the proximal end of the femur and the experience of the surgeons. The size of the femoral head, the ratio of head and neck diameter, and the shape of the neck of the femoral component have a substantial effect on the range of motion of the hip, the degree of impingement between the neck and rim of the socket and the stability of the articulation.[5] The present study aims at evaluation of the normal range of anterior and posterior neck length, the diameter of head and femur neck and the neck shaft angle of adult femora in South Indian population. The mean ANL & PNL in present study are 29.5 mm & 31.6 mm re-

spectively (table 2) that is similar to that obtained by D. Ravichandran et al[6] (average necklength – 31.88mm),Siwach[3] (average neck length is 37.2 mm). Ravi GO et al[7] found in their study that the average neck length of femur was 36.3+5.4mm. No significant difference observed among these parameters. The diameter of neck is 23.6mm in present study which is smaller than previous studies of India and outside India (table 3). Thus it is clear that the proximal femoral geometry varies among different ethnic groups.

Moreover it is observed from present study that the diameter of neck and cross sectional area of neck are lesser in South Indian population (table 3). Mishra A.K.et al[8] stresses that implant designs should be specific for Indian bones.The mobility of hip joints is also facilitated by the angle which allows the obliquity of the femur within the thigh and which helps the knees to be adjacent and inferior to trunk as stated by Ravi G O et al[7] . The neck shaft angle generally ranges from 115^0 to 140^0 in adults .The clinical importance of neck-shaft angle of femur lies in the diagnosis, treatment and follow-up of fractures of neck of femur, trochanteric fracture, slipped upper femoral epiphysis, developmental dysplasia, and any neuromuscular disorder involving of the lower extremities. According to K. L. Moore[9] neck shaft angle varies with age, sex and development of femur.

Table 2: Comparison of Present Studies with Other Studies in India

Different studies of India	Neck-shaft angle(degree)	Neck length (average) (mm)	Neck width (average) (mm)	DOH (mm)
Ravichandran et al	125-155 (commonly126.55)	31.88	30.99	-
RC Siwach,S Dahiya	114-136 (average123.5)	37.2	24.9	43.45
Ravi G.O. et al	136.8(average)	36.3+5.4	-	-
Present study	110-140 (average 126^0)	Anterior -29.5 Posterior-31.6	23.6	43.1

Table 3: Cross sectional area of femoral neck

Different study	Average neck diameter(mm)	Cross sectional area of neck(mm²)
Caucasian	31.5	778.92
Asian(Hongkong Chinese)	29	660.12
Previous study of India	28.39	633
Present study	23.6	437.21

N.B: Cross sectional area = $\pi(d^2/4)$ where d = diameter femoral neck

When this angle of inclination increased it is called coxavalga and when this angle decreased it is called coxavara. A varus angulation greater than 5° relative to the anatomic neck-shaft angle have been associated with an increased risk of implant failure as was reported by Chris Bailey[10].A.M. Fearon et al[11]evaluated by a prospective study that lower neck-shaft angle is a risk factor for greater trochanter pain syndrome in women.In present study the observed value of neck –shaft angle is 126^0. Other studies on neck-shaft angle reported by R.C.Siwach[3], D. Ravichandran[6], Saikia K.C.[12] showed values of 123.5^0, 126.55^0,139.5^0 respectively. The proximal femur acts as a brace, and its biomechanical properties depend on the width and length of the femoral neck. It also helps the limbs to swing clear of pelvis. The trans cervical region of neck is the narrowest portion of femoral neck and is of particular importance while fixing the fracture neck femur with screw as large diameter screw can decancellate the neck to ensue tamponade effect and cause avascular necrosis of head resulting in non union of fracture neck femur as observed by Mishra A.K.et al [8]who stresses that implant designs should be specific for Indian bones The availability of morphometric data describing the proximal femur allows guidelines to be developed for the functional dimension of femoral component as these anatomic data also allow assessment of the match between the shape of existing components and the proximal femur as stated by Reddy et al.[13]

CONCLUSION

The present study was conducted to see the morphometric dimensions of the proximal end of femur in South Indian population in order to utilize thisknowledge for the selection of appropriate prosthesis as well as for the pre-operative planning of hip replacement surgeries. Implants that are designed by taking in to account anthropometric and bio mechanic data will help in designing patient-specific implants thereby minimizing the complications. However maximum functional end result will be achieved only when the specific type of implants required are used.

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ORIGINAL ARTICLE

STUDY OF COMPARISON OF SERUM LIPID PROFILE, ELECTROCARDIOGRAPHICAL & ECHOCARDIOGRAPHICAL CHANGES BETWEEN EUTHYROID DIABETIC & HYPOTHYROID DIABETIC PATIENTS IN A TERTIARY CARE HOSPITAL, KOLKATA

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ABSTRACT

Introduction: Insulin and thyroid hormone metabolism and functions are dependent on each other. But the presence of hypothyroidism in type 2 diabetes mellitus patients and its impact on cardiovascular system are a less explored area. **Aim**: To compare the serum lipid profile, Electrocardiogrpathy & Echocardiographical changes between Euthyroid diabetic & hypothyroid diabetic patient and to document the difference in cardiovascular complications between these two groups.

Methodology: A cross-sectional observational study conducted on 100 Type 2 Diabetes Mellitus patients who were divided into euthyroid and hypothyroid diabetic group and were subjected to tests for dyslipedemia (Total Cholesterol, Triglyceride, HDL-C and LDL – C) and cardiological dysfunction using ECG and Echocardiography and the results were compared.

Results: 31% diabetic patients were hypothyroid and their mean cholesterol , triglyceride , Low density lipoprotein were 239.03 mg/dl , 181.35 mg/dl and 171.74 mg /dl respectively and hence found to be significantly increased as compared to euthyroid diabetic patients. In ECG, hypothyroid diabetic patients showed sinus bradycardia (32.6%) , low QRS voltage (19.35%) and increased QTc interval (16.13%). In Echocardiography , 9.68 % and 58.06 % hypothyroid diabetic patients had grade 2 and grade 1 diastolic dysfunction respectively with significant correlation.

Conclusion: Dyslipidemia with cardiological dysfunction is found to be more prevalent in hypothyroid (including subclinical hypothyroid) diabetes mellitus patients with significant association as compared to euthyroid diabetic patients.

Keywords: Type 2 Diabetes Mellitus, Hypothyroidism , Dyslipidemia , Diastolic dysfunction

INTRODUCTION

Diabetes and thyroid dysfunction are most common endocrinal disorders in adult population. Insulin & thyroid hormone metabolism can result in functional abnormalities of one-another. Hyperglycemia & hypothyroidism both act as an independent risk factor for ischaemic & non ischaemic cardiovascular diseases. Thyroid stimulating hormone (TSH) level is inversely related to Cell function. In subclinical hypothyroidism GLUT2 expression is reduced leading to insulin resistance i.e. further aggravating Type 2 diabetes mellitus (T2 DM) severity as well as complications. Hypothyroidism decreases inotropic & chronotropic effects thus reduces blood flow to tissue &

also causes left ventricular dysfunction. . Hypothyroidism is consistently associated with elevation of total & Low Density Lipoprotein (LDL) Cholesterol and triglyceride. . Electrocardiographical (ECG) changes include sinus bradycardia, increased PR interval, low amplitude of P wave & QRS complex, alteration of ST Segment, inverted T waves. T_2DM is associated with dyslipidemia which includes increased triglycerides, decreased High density Lipoprotein (HDL), increased LDL & increased apolipoprotein B. Myocardial Infaction(MI),stroke or non ischemic cardiovascular disease is the cause of death in upto 80% of patients with T_2DM. So the presence of hypothyroidism doubles the risk of cardiovascular

disease in T2DM patients.[1 – 4] This study intends to see the increased level of cardiovascular complications with this dual endocrinal disorder and to determine the prevalence of hypothyroidism in T2DM patients.

METHODOLOGY

The present study was a cross-sectional study, conducted at Medical college &hospital, Kolkata from January 2015 to July 2016 on 100 T2DM patients. T2DM with hyperthyroidism, T2DM patients with known structural heart disease, patients who were already taking hypolipidemic drugs, ACE inhibitors, anti anginal drugs, pregnant women, patients with infection, trauma, pre-existing liver/renal disease were excluded from the study group. In the study patients, thyroid status was found using clinical symptoms and signs, TSH and FT4 levels. The patients were then divided into euthyroid diabetic and hypothyroid diabetic group. They were subjected to tests pertaining to serum lipid profile, ECG and echocardiography. Dyslipidemia was considered to be present when the values of Serum cholesterol > 200 mg/dl , LDL > 100 mg/dl , Triglyceride > 150 mg/dl , HDL < 40 mg/dl (Men) and < 50 mg /dl (females). In echocardiography, parameters which were used were Ejection fraction, left ventricular internal diameter (diastolic&systolic), fractional shortening for systolic dysfunction. Mitral E & A velocity, ventricular E/A ratio, annular tissue motion(e '), isovolumetric relaxation time(IVRT) , Deceleration time(DT) & left atrial diameter were used for assessing diastolic dysfunction and staging was done accordingly EF<55% and FS <25% were taken as significant.

Diastolic dysfunction was staged as follows: **Stage 0(Normal)** - E/A ratio between 1 and 2, e'≥8-10, EDT between 150 and 190ms, IVRT between 60 and 90ms, and left atrial diameter (<4.1 cm in men and <3.9 cm in women). **Stage 1(Impaired Relaxation)** - E/A ratio <1 , e'≤8-10, E/e' ≤ 8 **Stage 2 (Pseudonormal)** - E/A ratio between 1 and 1.5 , e'≤8-10 , E/e' = 9 -12, IVRT > 90 ms Mild to moderate left atrial enlargement (4.1-5.1 cm in men and 3.9-4.6 cm in women). **Stages 3-4 (Restrictive)** - E/A ratio>1.5 , e'≤8-10, E/e'≥ 13 **and** At least two of the following: (a)EDT < l50ms (b) IVRT < 70 (c) severe left atrial enlargement (≥5.2 cm in men and ≥4.7 cm in women). The results of the tests were used to compare the serum lipid profile, ECG & Echocardiographical changes between euthyroid diabetic & hypothyroid diabetic patients and document the differences of cardiological dysfunction between these two groups and its association with hypothyroid state in Type 2 Diabetes Mellitus .Written informed consent was taken from patients and studied protocol was approved by institutional ethics committee for human research , Medical college Kolkata.

Statistical Analysis: Categorical variables were expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes. Continuous variables were expressed as Mean ± Standard Deviation and compared across the 2 groups using unpaired t test.The statistical software SPSS version 20 was used for the analysis. An alpha level of 5% wsa taken, i.e. if any p value is less than 0.05 it was considered as significant.

RESULT

In the present study of 100 Type 2 Diabetes Mellitus patients 51 patients were female and 49 were male patients whereas 69 patients (69%) were found to be euthyroid and 31 patients (31%) were hypothyroid in which 17 patients had subclinical hypothyroidism. Out of the 31 hypothyroid diabetic patients, 20 patients (64.52%) were female and rest 11 patients (35. 48%) were male. The mean age of euthyroid diabetic patients was found to be 44.96 years (± 2.79) where as hypothyroid diabetic patients mean age was 49.87 (± 2.99) years. Analysing the lipid profile of patients, the mean total cholesterol level in hypothyroid diabetic patients was found to be 239.03 mg/dl which was significantly increased (p < 0.05) compared to 199.7 mg/dl in euthyroid diabetic patients. 32.26 % hypothyroid diabetic patients had cholesterol level of >= 240 mg/dl (High level according to ATP III Classification of dyslipedemia) as compared to none being euthyroid diabetic . The mean LDL level of hypothyroid diabetic patients was found to be 171. 74 mg /dl as compared to 125.54 mg /dl in euthyroid diabetic.6.45 % patients of hypothyroid diabetes had LDL levels of >= 190 whereas none in euthyroid diabetic. The mean HDL level in hypothyroid diabetic patients was 31.03 mg/dl as compared to 40.5 mg/dl in euthyroid diabetic patients .The triglyceride level of hypothyroid diabetic patients was found to be increased with mean value being 181. 35 mg /dl as compared to 144.84 mg /dl in euthyroid diabetic patients. 45.16% patients of hypothyroid diabetes had triglyceride levels of >= 180 mg/dl mg/dl.

ECG study of the hypothyroid diabetic patients revealed sinus bradycardia (32.26%), low QRS voltage (19.35%), increased QT interval (16.13%), and ventricular premature complexes (9.68%) which showed significant association (p < 0.05) comparing to the euthyroid diabetic patients. ST depression was found in 12.9% and T inversion was present in 9.68 % of hypothyroid diabetes patients and no significant association (p >0.05) was found between ST- T changes in ECG and Thyroid status in diabetes.

In the echocardiographical evaluation of the patients of the study, it was found that the mean ejection

fraction in hypothyroid diabetic patients was 52.26% as compared to euthyroid diabetic patients where it was 59.1 %. The mean LVIDd(Left ventricular internal diameter end diastole) in hypothyroid diabetic patients was found to be 57.58 mm as compared to 54.26 mm euthyroid diabetic patients whereas the mean LVIDs (Left ventricular internal diameter end systole) in hypothyroid diabetic patients was found to be 42.42 mm as compared to euthyroid diabetic patients where it was 36.78 mm. The mean percentage of fractional shortening (FS) in hypothyroid diabetic patients (26.48 %) was found to be decreased as compared to hypothyroid diabetic patients(31) , 3 patients(9.68%) had grade II diastolic dysfunction , where as 18 patients(58.06%) had grade I diastolic dysfunction with a significant association (p < 0.05)

. The mean Mitral 'E' velocityin hypothyroid diabetic patients (70.39) was found to be decreased in hypothyroid diabetic patients as compared to euthyroid diabetic (85.62) whereas the mean Mitral 'A' velocityin hypothyroid diabetic patients (81.55) was found to be increased as compared to euthyroid diabetic patients (74.29). A decreased mean E/A ratio (velocity of diastolic early filling wave/velocity of late filling wave)inhypothyroid diabetic patients(0.88) was seen as compared to mean E/A ratio in euthyroid diabetic patients(1.16) .The study also revealed decreased Annular tissue motion (e') in hypothyroid diabetic patients(9.96) as compared to euthyroid diabetic patients (13.82) and increased mean E/e' ratio in hypothyroid diabetic patients (7.36) as compared to euthyroid diabetic patients (5.97) .

Table 1: Comparison of different parameters between euthyroid diabetic patients and hypothyroid diabetic patients

Factors	Thyroid Status (Mean ± Std. Deviation)		p-Value
	Euthyroid diabetic(n = 69)	Hypothyroid diabetic(n = 31)	
Age(years)	44.96 ± 2.79	49.87 ± 2.99	-
Weight (kg)	65.57 ± 2.13	68.58± 2.6	-
Height(cms)	159.97 ± 4.45	153.61± 2.65	-
BMI (kg/sqm)	25.65 ± 1.12	29.09 ± 1.52	-
SBP(mmhg)	138 ± 2.55	133 ± 3.24	-
DBP(mmhg)	76 ± 3.6	94 ± 2.7	-
HbA1c(%)	6.74 ± 0.1	7.16 ± 0.31	<0.001
TC(mg/dl)	199.71 ± 9.61	239.03 ± 9.73	0.012
TG (mg/dl)	144.84 ± 7.5	181.35 ± 3.67	<0.001
HDL(mg/dl)	40.51 ± 2.5	31.03 ± 2.12	0.034
LDL(mg/dl)	125.54 ± 5.37	171.74 ± 10.18	<0.001
EF(%)	59.1 ± 3.58	52.26 ± 4.58	0.002
LVIDd(mm)	54.26 ± 1.84	57.58 ± 2.94	0.003
LVIDs(mm)	36.78 ± 2.53	42.42 ± 4.36	0.013
FS(%)	32.9 ± 2.67	26.48 ± 4.08	0.002
E wave(cm/s)	85.62 ± 6.4	70.39 ± 12.79	0.003
A wave(cm/s)	74.29 ± 2.76	81.55 ± 6.27	0.034
E/A	1.16 ± 0.12	0.88 ± 0.22	0.012
e '(cm/s)	13.82 ± 1.85	9.96 ± 3.38	0.001
E/ e'	5.97 ± 0.44	7.36 ± 1.37	0.002
DT(ms)	186.12 ± 10.55	208 ± 21.08	0.003
IVRT(ms)	83.54 ± 9.23	98.65 ± 14.57	0.02
LA diam(mm)	38.13 ± 3.94	39 ± 4.34	0.325

Table 2: Distribution of ECG changes among euthyroid and hypothyroid diabetic patients

ECG changes	Thyroid Status		Total	p Value
	Euthyroid diabetic(n = 69)	Hypothyroid diabetic(n = 31)		
Low volt	0(0)	6(19.35)	6(6)	<0.001
Normal	54(78.26)	0(0)	54(54)	
QTc inc	0(0)	5(16.13)	5(5)	
Sinus brady	0(0)	10(32.26)	10(10)	
VPC	0(0)	3(9.68)	3(3)	

The mean Deceleration time in hypothyroid diabetic patients was found to be 208 milliseconds as compared to euthyroid diabetic patients where it was 186.12 milliseconds whereas the mean Isovolumic

relaxation time (IVRT) in hypothyroid diabetic patients was 98.65 milliseconds as compared to 83.54 milliseconds in euthyroid diabetic patients showing an increased deceleration time and Isovolumic relaxation time (IVRT) in hypothyroid diabetic patients. The mean Left atrial diameter was not found to be significantly associated between this two groups.

DISCUSSION

In the present study which comprised of 100 type 2 diabetes mellitus patients the prevalence of hypothyroid diabetic patients was found to be 31% (including 17 % subclinical hypothyroidism). The mean BMI in hypothyroid diabetic patients was found to be increased (29.09+1.52 kg/sq m) than euthyorid diabetic patients(25.65+1.12 kg/sq m).In hypothyroid diabetic patients the mean DBP (Diastolic blood pressure) was 94+2.7 mmhg whereas it was 76+3.5 in euthyroid diabetic patients. The Mean HbA1c levels in hypothyroid diabetic patients (7.16 +0.31%) was found to be increased than euthyroid diabetic patients (6.74 +0.1%) similar to the studies done by M. Anita Devi et al and Pasupathi et al.. Hence there is a presence of poor glycemic control in patients having both hypothyroid and diabetes in comparison to patients of diabetes mellitus alone. In hypothyroid diabetic patients mean cholesterol (239.03mg/dl), mean LDL (171.74) & mean triglyceride (181.35) was found to be significantly increased & mean HDL (31.03mg/dl) was found significantly decreased than euthyoid diabetic patients. A study by Prasanna K. Satpathy et alshowed mean Total cholesterol as 240.38 mg/dl, LDL as 144.13 mg /dl, HDL as 37.72 mg/dl and Triglycerides as 174.4mg/dl, and significant association with hypothyroid diabetes patients similar to the present study. ECG study of the hypothyroid diabetic patients revealed sinus bradycardia (32.26%), low QRS voltage (19.35%), increased QT interval (16.13%), and ventricular premature complexes (9.68%) which showed significant association (p < 0.05) comparing to the euthyroid diabetic patients. The study by Prasanna K. Satpathy et al, there was presence of sinus bradycardia (27.27 %), low voltage complexes (18.18 %), ventricular premature complexes (4.5 %), ST depression and T inversion (34 %) in patients of hypothyroidism. In echocardiographical study, the mean ejection fraction in hypothyroid diabetic patients was 52.26% whereas 59.1% in euthyroid diabetic patients. The mean percentage of fractional shortening (FS) in hypothyroid diabetic patients (26.48 %) was found to be decreased with a significatnt association (p < 0.05) as compared to mean FS in euthyroid diabetic patients (32.9%). Study by Prasanna K. Satpathy et al, the mean ejection fraction was found to be 55 %, mean LVIDd was 41.93 mm, mean LDIDs was 30.16 mm and mean percentage of fractional shortening was found

to be 28.53 %.[5,6] Hence the systolic dysfunction in the present study involving hypothyroid diabetic patients was found to be increasingly evident as compared to the above mentioned study. In hypothyroid diabetic patients (31), 3 patients(9.68%) had grade II diastolic dysfunction , where as 18 patients(58.06%) had grade I diastolic dysfunction with a significant association (p < 0.05). A decreased mean E/A ratio in hypothyroid diabetic patients(0.88) was seen with a significant association (p<0.05) as compared to mean E/A ratio in euthyroid diabetic patients(1.16).There was also significantly decreased annular tissue motion(e'),increased E/e`ratio, increased isovolumetric & decelaration time in hypothyroid diabetic patients as compared with euthyroid diabetic patient. A study by Prahlad Karki et al showed Diastolic dysfunction in 37.5% patients (15 patients out of total 40 patients). Of the patients of diastolic dysfunction, one had grade 2 diastolic dysfunction and the rest had grade 1 diastolic dysfunctions. Pericardial effusion in hypothyroid diabetic patients was 12.9% as compared to euthyroid diabetic patients (0%) where as in the study by Prahlad Karki et al, pericardial effusion was observed in 5 (12.5%) cases of hypothyroidism.It was seen that the dyslipedemia and cardiological dysfunction (Electrocardiological , systolic and diastolic dysfunction) is more prevalent in hypothyroid diabetes mellitus patients with significant association comparing with euthyroid diabetes mellitus patients.[6-9]

CONCLUSION

Hence as per the present study results thyroid dysfunction in Type 2 Diabetes Mellitus patients should be carried out annually with a systematic approach as per ADA guideline so that early intervention will reduce long term cardiovascular morbidity and mortality in these patients.

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